UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/070,566	03/07/2002	Mary Bendig	60816	6866

7590 07/01/2004

Peter G. Carroll
MEDLEN & CARROLL, LLP
101 Howard Street
Suite 350
San Francisco, CA 94105

EXAMINER	
MEHTA, ASHWIN D	
ART UNIT	**PAPER NUMBER**
1638	

DATE MAILED: 07/01/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/070,566	BENDIG ET AL.	
	Examiner	Art Unit	
	Ashwin Mehta	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 April 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-22* is/are pending in the application.

4a) Of the above claim(s) *20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-19 and 22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on *07 March 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group I, claims 1-19, 21 and 22 in the reply filed on April 12, 2004 is acknowledged. The traversal is on the ground(s) that the Examiner has not provided any appropriate explanation for separate classifications. This is not found persuasive because separate classifications were not required to be recited. The application was filed under 35 U.S.C. 371, and unity of invention rules were followed.

The requirement is still deemed proper and is therefore made FINAL. Claim 20 is withdrawn as being drawn to a non-elected invention.

Specification

2. The specification fails to comply with the sequence rules of 37 CFR 1.821-1.825. Sequences are recited on page 2, line 8, page 10, lines 8, 13, and 15, which must be referred to with their sequence identifiers. Figures 8A, 8B, 9, 10A, 10B, 11, 12, 13, 14A, and 14B each display sequences that also must be referred to by their sequence identifiers. The figures, or the brief descriptions of those figures on pages 12-13, must be amended to include the appropriate sequence identifiers.

3. Figures 3, 10, and 14 contain multiple views that are labeled with a letter. However, the brief descriptions of those figures in the specification do not recite those labels. The brief descriptions should be amended to recite the labels. See 37 CFR 1.74.

4. This application does not contain an abstract of the disclosure as required by 37 CFR 1.72(b). An abstract on a separate sheet is required. Note that the WO cover sheet of international patent publications are no longer accepted as abstracts by the USPTO for national stage applications.

Applicant is reminded of the proper language and format for an abstract of the disclosure. The abstract should be in narrative form and generally limited to a single paragraph on a separate sheet within the range of 50 to 150 words. It is important that the abstract not exceed 150 words in length since the space provided for the abstract on the computer tape used by the printer is limited. The form and legal phraseology often used in patent claims, such as "means" and "said," should be avoided. The abstract should describe the disclosure sufficiently to assist readers in deciding whether there is a need for consulting the full patent text for details. The language should be clear and concise and should not repeat information given in the title. It should avoid using phrases which can be implied, such as, "The disclosure concerns," "The disclosure defined by this invention," "The disclosure describes," etc.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground

provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

5. Claims 1-19, 21, and 22 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-7, 15, 20, 22-34 of U.S. Patent No. 5,958,422 ('422) in view of Liu et al. (Glycoconjugate J., 1995, Vol. 12, pages 607-617).

The claims are broadly drawn towards any chimaeric virus particle fro any plant virus having a coat protein with a beta barrel structure and modified by insertion of any immunologically active peptide of any tumor-associated mucin, at any immunologically effective site in the coat protein; or a method for producing said chimaeric virus particle; or any vaccine comprising said chimaeric virus particle.

'422 teaches particles of a plant virus containing a foreign peptide insert in the coat protein, wherein the coat protein has a beta-barrel structure, and the site of insertion is in a loop connecting beta sheets. The virus may be any plant virus, including RNA viruses, comoviruses, including cowpea mosaic virus (CPMV). The peptide can be incorporated in any exposed surface of the coat protein of the virus. The method of making the viral particles can comprise introducing a DNA sequence coding for the peptide into a cDNA sequence corresponding to the RNA of an RNA plant virus, inoculating plants, plant tissue, plant cells or protoplasts, optionally together with other RNA required for multiplication and assembly of the viral particle. The viral particle may be an immunogenic component of an antigenic complex. Liu et al. teach a peptide (identical to instant SEQ ID NO: 6) from the 20 amino acid repeats of the extracellular

portion of the MUC1 transmembrane protein, and that they generated highly specific immune responses recognizing mucin (pages 607-608, 611-613). Therefore it would have been obvious to modify the claimed virus particles, and method of making them, of '422 such that the foreign peptide inserted into the coat protein of the virus was the mucin peptide of Liu et al. One having ordinary skill in the art would have been motivated to do so given that the peptide of the viral particles of '422 could be any foreign peptide, including antigens, and that the viral particle could be the immunogenic component of an antigenic complex, and because Liu et al. teach that the mucin peptide generated specific responses to mucin. It also would have been obvious to insert the peptide into the C-terminus of the coat protein, including within 30 amino acids, as these are exposed regions of the protein. It also would have been obvious to insert the peptide into the S protein of cowpea mosaic virus, as this is one of the two coat proteins of the virus.

6. Claims 11-15 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-9 of U.S. Patent No. 5,874,087 ('087) in view of Liu et al. (Glycoconjugate J., 1995, Vol. 12, pages 607-617).

The claims are broadly drawn towards any chimaeric virus particle fro any plant virus having a coat protein with a beta barrel structure and modified by insertion of any immunologically active peptide of any tumor-associated mucin, at any immunologically effective site in the coat protein; or a method for producing said chimaeric virus particle; or any vaccine comprising said chimaeric virus particle.

'087 teaches a method of producing particles of a plant virus containing a biologically active peptide insert in the coat protein, wherein the coat protein has a beta-barrel structure, and

the site of insertion is in a loop connecting beta sheets. The virus may be any plant virus, including RNA viruses. The peptide can be incorporated in any exposed surface of the coat protein of the virus. The method of making the viral particles can comprise introducing a DNA sequence coding for the peptide into a cDNA sequence corresponding to the RNA of an RNA plant virus, inoculating plants, plant tissue, plant cells or protoplasts, optionally together with other RNA required for multiplication and assembly of the viral particle. The produced virus, or RNA therefrom, may be passaged in plants to produce further yields of virus. Liu et al. teach a peptide (identical to instant SEQ ID NO: 6) from the 20 amino acid repeats of the extracellular portion of the MUC1 transmembrane protein, and that they generated highly specific immune responses recognizing mucin (pages 607-608, 611-613). Therefore it would have been obvious to modify the method of making virus particles of '087 such that the biologically active peptide inserted into the coat protein of the virus was the mucin peptide of Liu et al. One having ordinary skill in the art would have been motivated to do so given that the peptide of the viral particles of '087 could be any biologically active peptide, and because Liu et al. teach that the mucin peptide generated specific responses to mucin.

7. Claims 1-1017-19, 21, and 22 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-18 of U.S. Patent No. 6,110,466 in view of Liu et al. (Glycoconjugate J., 1995, Vol. 12, pages 607-617).

The claims are broadly drawn towards any chimaeric virus particle fro any plant virus having a coat protein with a beta barrel structure and modified by insertion of any immunologically active peptide of any tumor-associated mucin, at any immunologically

effective site in the coat protein; or a method for producing said chimaeric virus particle; or any vaccine comprising said chimaeric virus particle.

'466 teaches particles of a plant virus containing a foreign peptide insert in the coat protein, wherein the coat protein has a beta-barrel structure, and the site of insertion is in a loop connecting beta sheets. The virus may be any plant virus, including comoviruses, including cowpea mosaic virus (CPMV). The viral particle may be an immunogenic component of an immunogenic composition. Liu et al. teach a peptide (identical to instant SEQ ID NO: 6) from the 20 amino acid repeats of the extracellular portion of the MUC1 transmembrane protein, and that they generated highly specific immune responses recognizing mucin (pages 607-608, 611-613). Therefore it would have been obvious to modify the claimed virus particles of '466 such that the foreign peptide inserted into the coat protein of the virus was the mucin peptide of Liu et al. One having ordinary skill in the art would have been motivated to do so given that the peptide of the viral particles of '466 could be any foreign peptide, including any antigen, and that the viral particle could be the immunogenic component of an immunogenic composition, and because Liu et al. teach that the mucin peptide generated specific responses to mucin. It would have been obvious to incorporate the peptide in any exposed surface of the coat protein of the virus, as the foreign peptide of the virus particle of '466 can be a biologically antigenic peptide, which must be presented. It also would have been obvious to insert the peptide into the C-terminus of the coat protein, including within 30 amino acids, as these are exposed regions of the protein. It also would have been obvious to insert the peptide into the S protein of cowpea mosaic virus, as this is one of the two coat proteins of the virus.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

8. Claim 22 is rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 1-19, 21, and 22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 1: the recitation, "immunogenically active peptide" in line 2 renders the claims indefinite. It is not exactly clear what peptides are encompassed by this recitation. All peptides, from any organism, may produce an immune response in some animal. Any peptide can be considered "immunologically active."

Further in claim 1: the recitation, "immunogenically effective" in line 3 renders the claims indefinite. It is not exactly clear what is meant by this recitation. What kind of immunogenic response is encompassed, T-cell response, B-cell response, etc.

In claim 4: the recitation, "within 30 amino acids, preferably within 15 amino acids" renders the claim indefinite. A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949).

In claim 6: the recitation, "the 20 amino acid repeat" renders the claim indefinite. It is not exactly clear what 20 amino acid repeat is being referred to. The claim indicates that it is from the extracellular portion of MUC1, and page 2, lines 7-8 of the specification shows a 20 amino acid sequence that is a repeat of the extracellular domain of a MUC1 protein. However, it remains that another MUC1 protein may have a different sequence, and while claims must be read in light of the specification, limitations of the specification cannot be read into claims. Page 10, lines 2-3 indicates that the same 20 amino acid sequence that appears on page 2 is set forth in

SEQ ID NO: 1 in the sequence listing. It is suggested that the recitation, --set forth in SEQ ID NO: 1-- be inserted into the claim in line 2 after, "repeat".

Further in claim 6: the recitation, "derived" renders the claim indefinite. It is not exactly clear what is meant by the recitation in the context of the claim. How is the peptide derived from the repeat? Is any sequence in the repeat changed to produce the peptide? It is suggested that the recitation be deleted.

In claim 7: the recitation, "the peptide is a 16-mer, preferably SEQ ID 6, or a 23-mer, preferably SEQ ID 7" renders the claim indefinite. Similar to the rejection of claim 4 above, the recitation presents a broad limitation together with a narrow limitation.

In claim 11: the recitation, "tumour-associated mucin peptide" renders the claim indefinite. There is insufficient antecedent basis for the limitation in the claim and claim 1. Claim 1 recites, "immunogenically active peptide of a tumour-associated mucin. However, claim 11 does not clearly indicate that the tumour-associated mucin peptide is the immunogenically active peptide recited in claim 1.

In claim 19: the recitation, "substantially" renders the claim indefinite. It is not clear what is encompassed by the recitation. When is the vaccine free of the adjuvant, as opposed to substantially free? The metes and bounds of the claim are unclear.

In claim 22: the claim provides for the use of a chimaeric virus particle, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 1-19, 21, and 22 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the chimeric virus particle of claim 1 and method of claim 11 wherein the peptide of the tumor-associated mucin is inserted in a loop connecting beta sheets and is free from flanking direct nucleotide sequence repeats, does not reasonably provide enablement for the claimed particle and method wherein the peptide is inserted at other sites in the coat protein. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The claims are broadly drawn towards any chimaeric virus particle fro any plant virus having a coat protein with a beta barrel structure and modified by insertion of any immunologically active peptide of any tumor-associated mucin, at any immunologically effective site in the coat protein; or a method for producing said chimaeric virus particle; or any vaccine comprising said chimaeric virus particle.

The specification indicates plant viruses with coat proteins having a beta barrel structure can be modified to be used as antigen-presenting carriers, by inserting an immunologically active peptide into the coat protein. The modification is carried out at the nucleic acid level, such that the peptide becomes inserted in loops of individual strands of the beta sheet of the coat protein in the assembled virus particle (page 3, lines 14-32). The coat protein of the cowpea mosaic virus

(CPMV) has two subunits, S (small) and L (large; page 5, lines 19-20). The specification teaches the construction of chimeric virus particles (CVPs) wherein peptides, set forth in SEQ ID NOs: 6 and 7, from the polymorphic epithelial cell tumor antigen, MUC1, were inserted into the viral particle such that the peptide is present in loops of the beta sheet of the S coat protein of CPMV (page 15, line 1 to page 16, line 5). Cowpea plants inoculated with the CVPs developed chlorotic lesions on the inoculated leaf and on secondary leaves, and spread through the plant in a manner similar to wild type CPMV (page 16, lines 6-31). Mice were immunized subcutaneously with one of the CVPs in adjuvant. Both of the CVPs elicited production of CPMV-specific and MUC1-specific antibodies (page 17, lines 4-15). Sera from mice immunized with the CVPs mouse E4 and human T47D tumor cells lines, which express MUC1 (page 17, line 17 to page 18, line 6). Mice immunized with the CVPs with and without adjuvant produced peptide titers that were not different from each other (page 20, lines 13-19).

However, the specification does not enable CVPs in which the mucin peptide was inserted in locations of the coat protein other than in loop regions connecting beta sheets, wherein the site is also free from flanking direct nucleotide sequence repeats. Porta et al. (Virology, 1994, Vol. 202, pages 949-955) also teach the development of plant viruses having a coat protein with a beta barrel structure for presentation of antigens. Porta et al. teach that CVP in which a peptide inserted into the βB-βC loop of the S capsid protein of CPMV retained the ability to infect plants. However, the lesions on the infected plants were smaller than those produced by wild type virus, the infection did not spread systemically through the plant, and the yield of virus particles was lower. Genetic analysis revealed that the constructs were reverting to wild type, deleting out the foreign peptide encoding sequences, due to the presence of directed

repeats flanking the insert (pages 951-955). Neither the prior art nor the specification teach CVPs in which the foreign peptide can be inserted into other sites of the coat protein. In the absence further guidance, undue experimentation would be required by one skilled in the art to determine other sites in coat proteins of plant viruses having beta barrel structures in which immunologically active peptides may be inserted. Given the breadth of the claims, unpredictability of the art and lack of guidance of the specification, undue experimentation would be required by one skilled in the art to make and use the claimed invention.

11. Claims 1-19, 21, and 22 are rejected. Non-elected claim 20 is withdrawn from consideration.

Contact Information

Any inquiry concerning this or earlier communications from the Examiner should be directed to Ashwin Mehta, whose telephone number is 571-272-0803. The Examiner can normally be reached from 8:00 A.M to 5:30 P.M. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Amy Nelson, can be reached at 571-272-0804. The fax phone numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and 703-872-9307 for After Final communications. Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished

applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

June 25, 2004

Ashwin D. Mehta, Ph.D.
Primary Examiner
Art Unit 1638